Remarks

Claims 1, 3-13, and 15-20 were pending. The Examiner has (improperly) added two obviousness rejections as well as a 112 rejection.

A. The Examiner Is Doing Piecemeal Prosecution – which is Improper

The Examiner has been handling this case since 2005, taking over from another examiner, who handled it in 2004. It is now 2008. This is NOT the time to be introducing new art rejections and 112 rejections. The MPEP is very clear. An Examiner may not continue to raise new issues in a piecemeal fashion:

> "Piecemeal examination should be avoided as much as possible. The Examiner ordinarily should reject each claim on all valid grounds available . . ."

See MPEP 707.07(g). In this case, the rejections are not prompted by amendments. The Examiner merely states that the rejections were prompted by "further consideration." (see Office Action, paragraph 6). This is improper.

B. The 112 Rejection Is Completely Unfounded

The Examiner's new 112 rejection is completely unfounded. The language is NOT duplicative. Step a(ii) merely provides the material, while step b involves oral administration to a subject. Step a(ii) does not say that the material is orally administered. However, step a(ii) does provides the antecedent basis *thereby making the claim clearer* – not indefinite. It is further pointed out that Claim 1 has not changed in this regard since it was filed in 2003.

Finally, the Examiner's 112 rejection is fatally flawed because the Examiner does not attempt to understand the claim by review of the specification. *E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1433 (Fed. Cir. 1988) ("It is entirely proper to use the specification to interpret what the patentee meant by a word or phrase in the claim."). Since it is clear from the specification what is intended, the Examiner's new 112 rejection is improper.

C. The Examiner Has Failed To Consider All Of The Claims

Applicants introduced Claims 15-20 in the prior response. Claim 15 uses the term "consisting." At no point in the Examiner's Office Action is this addressed. Rather, the Examiner continues to discuss "consisting essentially of" (see Office Action, bottom of page 3). Where is the discussion of "consisting"? The Examiner either overlooked Claim 15 or has improperly ignored it. Importantly, by using "consisting," Claim 15 excludes other steps.

To further the prosecution, Applicants have also added Claim 21, which depends on Claim 8. This underscores Applicants' previous argument concerning "consisting essentially."

D. The Examiner Has Failed to Consider ALL Of The Evidence

In the prior response, Applicants noted the materials from the Arizona Department of Health concerning *C. perfringens*. Applicants argued that the complete lack of oral therapy in the document is evidence of non-obviousness. The Examiner fails to even mention this evidence and argument. This is improper. The Examiner must address each and every piece of rebuttal evidence. Indeed, the analysis must start over, as stated in *In re Rinehart*, 531 F.2d 1048, 1052, 189 USPQ 143, 147 (CCPA 1976), "[w]hen . . . evidence is submitted in rebuttal, the decision-maker must start over . . . An earlier decision should not, as it was here, be considered as set in concrete." See also *In re Piasecki*, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984) ("the examiner must consider all of the evidence anew.").

E. The Examiner Has Failed To Address The Central Argument Made By Applicants

In the prior response (at the bottom of page 6), Applicants challenged the Examiner's combination of references by pointing out that common sense would dictate antibiotic treatment – not oral antibodies:

> "Thus, one skilled in the art would ask: do I want to use antibiotics or do I want to resort to this time-consuming method of the '018 Patent? Common sense dictates that antibiotics are the easier route than what is offered by the '018 Patent and thus the practical route for food poisoning. There is no rational underpinning

> to support the Examiner's combination or conclusion that an antibody based approach for *C. perfringens* is obviousness. One skilled in the art would simply view the '018 Patent approach to be not practical. (See Second Declaration of Dr. Stafford, paragraph 5)."

Thus, Applicants central argument (supported by the declaration) was that while antibiotics might be obvious, the particular references cited certainly did not make oral antibody therapy for *C. perfringens* obvious. The Examiner is reminded that the '018 Patent does not mention *C. perfringens*. The Uemura reference and the Merck reference do not teach oral therapy for *C. perfringens*. Applicants argued that there is nothing in the Uemura reference or Merck reference that would cause one skilled in the art to resort to the IMPRACTICAL teachings of the '018 Patent.

The only possibly responsive statement by the Examiner is the statement that in the Merck reference "antitoxin is used (p.1178, of record, in particular)." (Office Action, page 4). But this completely misses the point! Dr. Stafford's Declaration specifically noted that the antitoxin treatment for tetanus discussed in the Merck document was NOT oral. (See the Second Declaration, paragraph 6). Turning to page 1178 (cited "in particular" by the Examiner), one finds antitoxin discussed in the context of tetanus only in the context of parenteral therapy (e.g. IM injections) – just as Dr. Stafford pointed out!

Applicants previously stressed (also on page 6) that the Merck reference provides a DIFFERENT solution for *C. perfringens*:

> "The Examiner is <u>not</u> free to ignore the fact that the Merck Manual suggests a <u>different</u> solution for *C. perfringens*, namely antibiotics."

The Examiner is reminded that the Examiner cannot rely on material that is OUT OF CONTEXT and ignore material that is IN CONTEXT. The antitoxin therapy of tetanus discussed in the Merck reference, since it is for a different organism and is NOT oral, is OUT OF CONTEXT. The treatment for *C. perfringens* – which is IN CONTEXT – is antibiotics. The Examiner cannot pick and choose bits of unrelated material, to the exclusion of the relevant teachings in the Merck reference:

> "It is impermissible, within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art."

In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965) [Cited in *In re Hedges*, 228 USPQ 685, 687 (Fed. Cir. 1986)].

Thus, the central argument, that nothing in the Merck reference would cause someone skilled in the art to do anything except treat *C. perfringens* with antibiotic, has been side-stepped and remains unaddressed by the Examiner. This is fatal to the Examiner's obviousness rejection based on these references. There is nothing in the record that serves as a legitimate BASIS for combining the references. This is a critical pre-requisite; absent a basis for making the combination, the obviousness rejection cannot stand. *See In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) ("the Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and combine them").

F. The '299 Patent Teaches Away

As noted earlier, the Examiner has added two new obviousness rejections, relying on the '299 Patent together with other art. In addition to being untimely, the rejections are completely unsupportable. The '299 patent focuses on the then emerging use of monoclonal antibodies as replacements for polyclonal antibodies (notably for therapy of acute bacterial toxicity such as tetanus and diphtheria). Numerous statements made by the '299 inventors emphasize the inadequacy of polyclonal antibodies. Thus, rather than supporting the Examiner's argument, it undermines it. The '299 patent repeatedly teaches away from the use of polyclonal antibodies.

> [Column 2; lines 43-46] Monoclonal antibodies are replacing conventional antisera in diagnostic laboratories and are providing new insights in medicine
>
> [Column 3; lines 9-18] Thus, the resulting antiserum reflects the contribution of **multiple antibody-secreting clones that contribute both desired and undesired antibodies**. [emphasis added] These undesirable antibodies must then be absorbed from the antiserum to prevent interference with its intended use. Conventional antisera is difficult to reproduce because individual animals respond unpredictably with varying proportions of antibody of different activity and specificity; therefore, supplies are often limited.

[Column 3; line24-28] Hybridoma antibody technology . . . has the distinct **advantage** of allowing the use of complex unpurified antigens [emphasis added]

[Column 9; lines 41-46, discussing the use of polyclonal antisera for tetanus treatment] A major **disadvantage** of equine anti-toxin antibodies is that their use can result in serum sickness . . . [emphasis added] For this reason, horse antisera are no longer prevalently in use. . . [Column 9; lines 53-63, here the inventors go on to suggest that human antisera would be a better alternative to heterologous antisera, but there remain problems with polyclonal therapy] While the risk of serum sickness is reduced by using human polyclonal antibodies, there are other inherent problems, in addition to expense, associated with their use. . . lot-to-lot variation . . . transferring contaminants and disease-causing agents . . . the need to immunize humans.

[Column 11; lines 23-29, the inventors describe the methods and drawbacks of polyclonal treatment in diphtheria] Allergic sensitivity to horse serum proteins must nevertheless be assessed prior to administration of the antitoxin. Obviously, this can delay treatment. Moreover, lack of immediate allergic reaction does not negate the possibility of long term adverse reaction, such as serum sickness. Use of horse antisera poses the same disadvantages discussed for tetanus antitoxin . . .

[Column 12; lines 23-35, the inventors teach the problems associated with polyclonal antibody production] This [monoclonal antibody therapy] is a distinct **advantage** over the traditional technique of raising antibodies in immunized humans and animals where the resulting sera contain **multiple antibodies of different specificities that vary in both type and titer with each animal** and, in individual animals, with each immunization. [emphasis added] Furthermore, animal sera require extensive purification to remove contaminants that can cause serum shock upon administration to humans; such procedures can add to the cost of traditional polyclonal antibodies. Even when human antisera are used, there may still be the problem of serum contaminants or inadequate supply.

The Examiner asserts that the disclosure in Columns 11 and 12 of the '299 Patent make obvious the instant invention. Quite the contrary, as shown above the '299 inventors make it quite clear that polyclonal antibody strategies should be avoided for their stated reasons. The Examiner also cites Table 1 of the '299 patent as anticipating our polyclonal antibodies. This is incorrect and misleading. The paragraph referencing Table 1 discusses the applications were human monoclonal antibodies could be employed ([Column 11; lines 62-66] The invention encompasses the extension of the human-rodent hybridoma technique to the production of human monoclonal antibodies against other icrobial [sic] toxins including, but not limited to, the exotoxins listed in Table 1 . . .).

By pointing to the advantages of monoclonal antibodies over polyclonal antibodies, the '299 Patent teaches away from the polyclonal avian antibodies presently claimed:

> "A reference may be said to teach away when a person of ordinary skill, upon [examining] (sic) the reference, . . . would be led in a direction divergent from the path that was taken by the applicant."

Para-Ordnance Manufacturing v. SGS Importers International, 37 USPQ2d 1237,1241 (Fed. Cir. 1995) (quoting *In re Gurley*, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994)). Clearly, one skilled in the art, upon reading the MANY statements in the '299 Patent (quoted above) about the advantages of monoclonal antibody technology and disadvantages of polyclonal antibodies, would be led in a direction AWAY from polyclonal antibodies. To underscore the nature of the antibodies claimed, Claim 15 has been amended to specify that the avian antibodies are "egg" antibodies, which are by nature polyclonal. Support for "egg" antibodies is found in numerous places in the specification, including but not limited to, page 9, lines 6-19.

When the '299 Patent is correctly assessed for the MANY statements (quoted above) made against non-monoclonal approaches, it is clear that it CANNOT be combined with non-monoclonal art, which is what the Examiner has done. Such references are completely incompatible. Moreover, such statements (including but not limited to statements about "undesired antibody") indicate a belief that there is a poor likelihood of success.

CONCLUSION

Applicants believe that the arguments and evidence set forth above traverse the Examiner's rejections and, therefore, request that these grounds for rejections be withdrawn for the reasons set forth above. The Examiner is reminded that PTO decisions are reviewed using the standard set forth in the *Administrative Procedure Act*, 5 U.S.C. § 706. *Dickinson v. Zurko*, 527 U.S. 150, 154 (1999). Under that statute, actions are set aside that are arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law. Moreover, factual findings are set aside that are unsupported by substantial evidence. *In re McDaniel*, 293 F.3d 1379, 1382 (Fed. Cir. 2002).

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.984.0616.

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